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VIA FACSIMILE:
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Date: March 20, 2003

To: UNITED STATES PATENT AND TRADEMARK OFFICE
Attention: Examiner Sharareh Fax No. (703) 746-3136
Group 1619 (Direct)

Re: Applicant : Alice C. MARTINO et al
For : TABLET FORMULATION
Serial No.: 09/656 364
Filed : September 6, 2000
Our Ref. : Pharmacia Case 6107.N CN2

SUPPLEMENTAL AMENDMENT AND
SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Dear Examiner Sharareh:

As discussed during our telephone conversations on March 3, 2003 and March 19, 2003, I am enclosing a copy of a Supplemental Information Disclosure Statement, with attached U.S. Patent 5 591 714 (the '714 patent). This patent is the U.S. equivalent of Russian patent RU 2053240 which has been cited by the Euroasian Patent Office during the examination of the corresponding Euroasian patent application.

The inventors have reviewed the '714 patent. Based upon that review, it is submitted that the patent neither anticipates nor renders obvious the claims of this invention for the following reasons:

The '714 patent is directed to compounds that are useful as antibiotics and to compositions containing said compounds. The compositions can contain conventional excipients and carriers such as binders, disintegrants, lubricants, flavoring agents and coloring agents and tablet formulations thereof are prepared by conventional techniques. The compounds are water soluble and there is no evidence that a supersaturated state is generated with the compounds in the '714 patent and, likewise, there is no evidence that enhanced drug absorption is achieved on addition of a binder, such as HPMC, to the tablet formulations therein.

09/656,364

Furthermore, the amount of croscarmellose sodium or other superdisintegrant required in the claimed tablet composition is 6 to 40%, whereas the only amount disclosed in the '714 tablet composition is 3.1%.

The compound of special interest in the '714 patent is identified as Compound 38. Compound 38 is a di-chloro and octyl containing analog of A82846 which, in turn, is an analog of vancomycin. Vancomycin is a highly water soluble drug with a reported solubility of >100 mg/ml in water (see: Merck Index, 13th Edition). Compound 38 and the related chloro/octyl (C8) analogs of A82846 are also water soluble as evidenced by the following excerpts.

Compound 38 is water soluble as shown in column 21, lines 31-33 ***in the '714 patent, wherein it is stated that:***

> ***"This solution (of Compound 38) was evaporated to dryness in vacuo, the residue was treated with water 50 ml, and a few drops of n-butanol and lyophilized".***

Similarly, the mono-chloro/octyl (C8) analog of A82846 (Compound 1) is also water soluble as shown in column 21, lines 3-5 ***in the '714 patent wherein it is stated that:***

> ***"The reaction solution was concentrated in vacuo, the residue (Compound 1) was diluted with water (i.e., dissolved), 25 ml, and this solution was lyophilized".***

Likewise, the other related analogs of A82846 that are structurally similar to Compound 38 are also water soluble as shown by Compound 28 wherein the octyl group in Compound 38 is replaced with a phenylpropionyl moiety in Compound 28 and, as shown on column 21, lines 47-49 ***in the '714 patent, it is stated that:***

> ***"The solution was evaporated to dryness in vacuo; the residue (Compound 28) was treated with water (i.e., dissolved) and lyophilized".***

Likewise, the heptanoyl analog, Compound 69 is also water soluble as shown in column 21, lines 66-67, ***in the '714 patent wherein it is stated that:***

59/656 364

> ***"The solution was evaporated to dryness in vacuo; the residue (Compound 69) was treated with water (i.e., dissolved) and lyophilized."***

The water solubility of Compound 38 and related compounds is an important point because, obviously, a supersaturated state cannot be generated if the compound is already water soluble. Thus, the compounds of the '714 patent are not rapidly precipitating compounds, a requirement of the instant claim.

In addition to not disclosing a rapidly preciptitating drug as required by the instant claims, the '714 patent does not teach or suggest the use of a superdisintegrant in the amount of 6% to 40% by weight of the composition. In the only tablet formulation described in the '714 patent, Example 8, column 24, lines 30-43, the amount of superdisintegrant croscarmellose sodium, is about 3.1%. This is well below the amount required by the claimed tablet composition.

CONCLUSIONS

The compounds disclosed in the '714 patent are water soluble and hence are incapable of forming a supersaturated state by formulations containing polymeric binders such as HPMC. Furthermore, the claimed tablet composition requires that a superdisintegrant be present in amount of 6% to 40% whereas the '714 tablet formulation does not.

Thus, the '714 patent does not teach how to improve the oral absorption of soluble salts of poorly soluble drugs or poorly soluble anhydrous forms of hydrate-able non-ionizable drugs by generating solid powders capable of forming a supersaturated state on contact with water or simulated physiological fluid, and thereby improving the oral absorption of the class of drugs defined in the instant claims.

Respectfully submitted,

Sidney B. Williams, Jr.

09/656 364

Encl.: Supplemental Information Disclosure Statement, with Form PTO-1449
Copy of U.S. Patent No. 5 591 714

cc: John Engelmann
Encl.: Same

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper and the above-listed enclosures (if any) is being facsimile transmitted to the Patent and Trademark Office on the date shown below.

Signature Susan G. Padgham **Date** March 20, 2003
Susan G. Padgham

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PATENT APPLICATION

IN THE U.S. PATENT AND TRADEMARK OFFICE

March 19, 2003

Applicant(s): Alice C. MARTINO et al.

For: TABLET FORMULATION

Serial No.: 09/656 364 Group: 1617

Confirmation No.: 3730

Filed: September 6, 2000 Examiner: S. Sharareh

Atty. Docket No.: Pharmacia Case 6107.N CN2

Assistant Commissioner for Patents
Washington, DC 20231

SUPPLEMENTAL INFORMATION DICLOSURE STATEMENT

Sir:

In compliance with the provisions of Rules 1.97 and 1.98, enclosed and listed on Form PTO-1449 is a copy of U.S. Patent No. 5 591 714.

The fee for filing this information disclosure statement is $180.00. Authorization to debit Deposit Account No. 06-1382 in the amount of $180.00 is hereby given. More specifically, the enclosed reference is the U.S. equivalent of Russian Patent RU 2053240, cited in the report of the Eurasian Patent Office during prosecution of the corresponding Eurasian application.

Respectfully submitted,

Sidney B. Williams, Jr.

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Encl: Form PTO-1449, and one copy of listed reference

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